IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF NEW MEXICO

MARK GILBERT RIMBERT, individually,
and as Personal Representative of the Estates
of GILBERT JOHN RIMBERT, and
OLIVIA ACOSTA RIMBERT, deceased,

Plaintiff,

vs. No. CIV 06-0874 JB/LFG

ELI LILLY AND COMPANY,

Defendant.

MEMORANDUM OPINION AND ORDER

THIS MATTER comes before the Court on Defendant Eli Lilly and Company's Motion to Exclude Expert Testimony of Dr. Grace Jackson, filed March 20, 2008 (Doc. 58)("Motion"). The Court held a hearing on June 27, 2008. The primary issue is whether the Court should, under the requirements of Daubert v. Merril Dow Pharmaceuticals, Inc., 509 U.S. 579, 589-98 (1993), exclude the opinions of Plaintiff Mark Gilbert Rimbert's identified expert, Grace Jackson, M.D. Because the Court finds that Jackson's opinions are based on a sufficiently reliable methodology, the Court will deny the motion.

FACTUAL BACKGROUND

Dr. Jackson is a board-certified psychiatrist and has prescribed Prozac to many patients. She does not, however, know of any patient who has attempted or committed suicide, or committed homicide, while taking Prozac. Unfortunately, the incident that gave rise to this lawsuit involved a patient who killed his wife, his dog, and himself.

1. Dr. Jackson's Background.

Dr. Jackson has a B.S. in Biology and an M.D. from University of Colorado Health Sciences Center. See Exhibit A to Response, Curriculum Vitae of Jackson at 1 ("Curriculum Vitae"). She is a board-certified psychiatrist. See id. She completed a psychiatric residency at the Malcolm Grow, National Naval, and Walter Reed Army medical centers. See id. at 2. She has experience as a staff psychiatrist, forensic consultant, and private practicioner. See id. at 2-3. Dr. Jackson has published articles on psychiatric drugs and their use. See id. at 8-10.

Dr. Jackson has proscribed Prozac to "hundreds" of patients – the last time she prescribed Prozac to a patient was sometime before April of 2002 – but she knows of no patient who has attempted suicide, completed suicide, or committed homicide while taking Prozac. See Exhibit A to Motion, Deposition of Grace E. Jackson, M.D. at 48:19-24 (taken December 13, 2007)("Jackson Depo."); id. at 51:1-53:20. Jackson does not hold herself out to be an expert on homicide-suicide. See id. at 59:3-13.

Dr. Jackson has been an expert witness and consultant for Mark Rimbert's counsel, Vickery, Waldner & Mallia, from November 2006 through the present. See id. at 6. Dr. Jackson is a full-time employee of Mark Rimbert's counsel, Mr. Andy Vickery, and his firm. See Exhibit B to Motion, Deposition of Dr. Jackson at 61:1-3 (taken December 11, 2007)("Second Jackson Depo."). She has worked full time for Mr. Vickery's firm since approximately November of 2006. See id. at 61:4-8.

2. Incident Giving Rise to the Lawsuit.

On or about September 25, 2003, Gilbert Rimbert, who suffered from depression and had been prescribed Prozac, shot and killed his wife Olivia, the family dog, and himself. See Defendant Eli Lilly and Company's Memorandum in Support of Its Motion to Exclude Expert Testimony of

Dr. Grace Jackson at 1, filed March 20, 2008 (Doc. 59)("Memo. in Support of Motion to Exclude"). Defendant Eli Lilly and Company manufactures and markets Prozac. At the time it was prescribed for Gilbert Rimbert, Prozac was a prescription antidepressant medication that the United States Food and Drug Administration ("FDA") had approved for use in the treatment of major depressive disorder. See Defendant Eli Lilly and Company's Memorandum in Support of its Motion for Summary Judgment on all Claims ¶ 2, at 5, filed March 19, 2008 (Doc. 56)("Memo. in Support of Motion for Summary Judgment"); Exhibit A to Memo. in Support of Motion for Summary Judgment, Declaration of John M. Plewes, II, M.D. at 3 (taken March 11, 2008)("Plewes Decl."); Exhibit A to Memo. in Support of Motion for Summary Judgment, Package Insert for Prozac ("Prozac Insert"). Fluoxetine is the generic name for Prozac. See Exhibit C to Memo. in Support of Motion for Summary Judgment, Deposition of Barry Hochstadt, M.D. at 23:6-10 (taken August 15, 2007)("Hochstadt Depo."). Mark Rimbert alleges that Eli Lilly knew "long before the public brouhaha" that it was possible to design a safer Prozac. See Complaint ¶ 13, at 5. Mark Rimbert contends that: "Gilbert Rimbert's death fits the 'signature pattern of [selective serotonin reuptake inhibitors ("SSRI")]-induced suicide which Dr. Beasley and other Lilly scientists observed in 1991." Id. ¶ 46, at 14. Specifically, Mark Rimbert contends that Eli Lilly's failure to use due care proximately caused the deaths of Gilbert and Olivia Rimbert. See id. ¶¶ 49, 51, 53 & 55, at 15-16.

PROCEDURAL BACKGROUND

Mark Rimbert has brought this products liability suit against Eli Lilly, contending that Prozac caused Gilbert Rimbert to kill his wife, his dog, and himself. Mark Rimbert designated Dr. Jackson as his expert. Eli Lilly has challenged Dr. Jackson's methodology for arriving at her opinion under Daubert v. Merrell Dow Pharmaceuticals, Inc.

1. Mark Rimbert's Claims.

Gilbert Rimbert's son, Mark Rimbert, filed this products liability, personal injury, and wrongful death lawsuit against Eli Lilly. See Complaint ¶ 1, at 1 (filed September, 18, 2006)(Doc. 1)("Complaint"). Mark Rimbert alleges that Prozac caused Gilbert Rimbert to kill his wife, his dog, and himself. Mark Rimbert has designated Dr. Jackson as an expert, to be called at the trial to offer her opinion regarding the role Prozac played in Gilbert Rimbert's tragic last acts of shooting his wife and dog, and then himself.

2. Dr. Jackson's Conclusions.

In her report, Dr. Jackson stated that Gilbert Rimbert's psychic pain, which was the result of his spouse's rejection, "became obsessive and psychotic under the influence of Prozac." Exhibit B to Plaintiff's Memorandum in Opposition to Defendant's Motion to Exclude Dr. Grace Jackson at 50 (filed April 17, 2008)(Doc. 75)("Report"). She also stated:

> I believe it would be incorrect to suggest that Prozac was the necessary and sufficient cause of the deaths of Gilbert and Olivia Rimbert, and their pet dog (Ivy). However, in the context of Gilbert's pre-existing risk factors for suicide and homicide, and in the context of his diminished capacity to resist them, it is more likely than not true that Prozac converted a case of probable dysthymia into a case of agitated depression with obsessive and psychotic features. In this sense, Prozac was the definitive, contributive cause of the Rimbert tragedy.

Id. In an affidavit filed after submitting her report and being deposed, Dr. Jackson attempted to clarify the conclusions that she set forth in her report. See Affidavit of Grace E. Jackson, M.D. at 4 (executed May 14, 2008)(filed May 22, 2008)(Doc. 99)("Jackson Aff."). She maintained that her original report and testimony are consistent in supporting the conclusion that "Prozac [was] the linchpin of the Rimbert tragedy." Id. Dr. Jackson also argued that "[i]t was against a complex backdrop of personal and familial circumstances, but within a progressive chain of events, that Prozac proved to be the clincher." Id. Finally, in her deposition testimony, Dr. Jackson stated her

belief that, to a reasonable degree of medical certainty, Prozac contributed to Gilbert and Olivia Rimbert's deaths. See Jackson Depo. at 359-60.

> Q: Is it your opinion in this case to a reasonable degree of medical certainty and/or probability that Prozac contributed to the deaths of Olivia and Gilbert Rimbert?
>
> A: Yes it is.
>
> Q: Okay, and when you were formulating your opinions in this case, did you consider the fact that Prozac may have had absolutely nothing to do with their deaths?
>
> A: I sure did.

Id.

3. Dr. Jackson's Methodology.

In reaching her conclusion about Prozac's role in Olivia and Gilbert Rimbert's deaths, Dr. Jackson outlined her reasoning for general causation and specific causation in her report. See Exhibit B to Plaintiff's Memorandum at 33 & 38. In her section on general causation, Dr. Jackson relied on two peer-reviewed scientific papers to support a finding that Prozac has a "propensity . . . to induce suicidality." Report at 33. Those two papers are the Cusin article, Exhibit E to Motion, C. Cusin, M. Fava, J.D. Amsterdam, F.M. Quitkin, F.W. Reimherr, C.M. Beasley, Jr., J.F. Rosenbaum, & R.H. Perlis, Early Symptomatic Worsening During Treatment With Fluoxetine in Major Depressive Disorder: Prevalence and Implications, 68:1 J. Clinical Psychiatry 52-57 (2007)("Cusin article"), and the Perlis article, Exhibit F to Motion, R.H. Perlis, C.M. Beasley, Jr., J.D. Wines, Jr., R.N. Tamura, C. Cusin, D. Shear, J. Amsterdam, F. Quitkin, R.E. Strong, J.F. Rosenbaum, M. Fava, Treatment-Associated Adverse Effects in an Open, Multicenter Trial of Fluoxetine for Major Depressive Disorders, 76 Psychotherapy & Psychosomatics 40-46 (2007)("Perlis article"). Dr. Jackson alleges that the two complimentary papers "reveal the

astoundingly high prevalence of suicide and worsening of depression during the early course of treatment." Id.

The first paper, the Cusin article, involved, after exclusions, 694 participants who were placed on Prozac treatment for twelve weeks. The authors of the study observed "clinical worsening" – in other words, increased depression – in 39% of participants. Id. at 34. The second paper is a retrospective review of the same study. Id. at 35. The paper showed that, after three months, 14% of participants who started Prozac therapy without suicidality became suicidal. Id. at 36. In her report, Dr. Jackson noted that the authors of the second paper applied a "Cox regression model" to demonstrate that "activiation (agitation, nervousness, and/or akathisia) and early clinical worsening were both significantly associated with the emergence of suicidality." Id. at 36.

The second important component of Dr. Jackson's general causation analysis is the connection between SSRIs and akathisia, and the connection of akathisia and dysphoria, irritability, aggression, or suicide attempts. See id. at 37. Dr. Jackson contended in her report that SSRIs may cause akathisia, and that akathisia could, in turn, cause aggression and suicidality. Dr Jackson cites the DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS at 801 (4th ed. American Psychiatric Society, 2000)(DSM)[1] to support her contention. See Report at 37. Dr. Jackson observed that "it is essential for clinicians to recognize the possibility that suicide and/or homicide may become attractive 'solutions' to the unrelenting psychic distress of akathisia." Id. at 37 (citations omitted)(emphasis in original). In other words, with respect to general causation, Dr. Jackson found that Prozac creates a risk of suicide and homicide.

[1] According to the American Psychiatric Association, the Diagnostic and Statistical Manual of Mental Disorders is "the standard classification of mental disorders used by mental health professionals in the United States." American Psychiatric Association, http://psych.org/MainMenu/Research/DSMIV.aspx (last visited September 25, 2008).

For specific causation, Dr. Jackson explored three factors: (i) Pharmacodynamics – what Prozac does to the brain, (ii) Pharmacokinetics – what the body does to Prozac, and (iii) Unique biology – how Gilbert Rimbert's physiology was unique. Dr. Jackson relied on human and animal studies, as well on knowledge of the chemical components of SSRIs in making this exploration. Under the first factor – pharmacodynamics – Dr. Jackson referred to investigations that have "universally demonstrated serotonin reuptake inhibitors – in patients and healthy controls – trigger significant and prolonged reduction in the serotonin metabolite known as 5HIAA."[2] Report at 38. This phenomenon "has been shown to reflect a decrease serotonin turnover (i.e., less serotonin breakdown because of diminished serotonin production and release)." Id. (emphasis in original). Moreover, Dr. Jackson maintains that low levels of 5HIAA have been "consistently found in the cerebrospinal fluid of patients and perpetrators of impulsive acts, including arson, homicide, and suicide." Id. Dr. Jackson also refers to animal studies that corroborate this evidence, and concludes that serotonin reuptake inhibitors "appear to induce long-lasting vulnerability within the serotonin pathways of the brain – a perturbation which likely increases the risk of chronic and/or recurrent depression and anxiety." Id. at 44.

In analyzing the second and third factors – pharmacokinetics and Gilbert Rimbert's unique physical characteristics – Dr. Jackson observed that Gilbert Rimbert may have suffered from an "atypical accumulation of Prozac within the brain (i.e., enhanced akathisia and dysphoric effect)." Id. at 48. She explained that this accumulation in the brain may have resulted from how the body metabolizes Prozac, and the interaction of Gilbert Rimbert's physical characteristics, including his diabetes, fatty liver, and other ailments. Id. Dr. Jackson observed that

[2] 5HIAA – 5-hydroxyindole-acetic acid – is a metabolite of serotonin.

> Prozac has an intrinsically long half-life, which contributes to the delayed onset of adverse drug effects. Gilbert Rimbert may have been especially sensitive to the initial dose of Prozac. . . . The effects of this dose would not have equilibrated by the time of his three wekk follow-up on 9/9/03. Subsequently, when the dose of Prozac was doubled, he was exposed to a precarious surge in the blood and brain levels of the SSRI."

Report at 48. To support the assertion that Prozac exacerbated Gilbert Rimbert's pre-existing medical conditions, Dr. Jackson again cited scientific articles and abstracts, including, among others, C. Jongen, J. van der Grond, L.J. Kappelle, G.J. Biessels, M.A. Viergever, J.P.W. Pluim, et al., Automated Measurement of Brain and White Matter Lesion Volume in Type 2 Diabetes Mellitus [abstract], 50 DIABETOLOGIA 1509 (2007); A. Degroot & G.G. Nomikos, Fluoxetine Disrupts the Integration of Anxiety and Aversive Memories [abstract], 30 NEUROPSYCHOPHARMACOLOGY 391 (2005); J. Vevera, Z. Fisar, T. Kvasnicka, H. Zdenek, L. Starkova, R. Ceska, and H. Papezova, Cholesterol-lowering Therapy Evokes Time-limited Changes in Serotonergic Transmission [abstract], 133 PSYCHIATRY RESEARCH 197 (2005).

The technique that Dr. Jackson used to analyze these three factors is known as differential diagnosis. This diagnosis operates by first "ruling in" all possible causes for the outcome at issue – in this case, the murder-suicide. The expert then uses valid scientific techniques to eliminate possible causes. By applying differential diagnosis and analyzing the three factors in her special causation section, Dr. Jackson found that Gilbert Rimbert's violence and suicide arose from "a constellation of pharmacokinetic and biological variables." Id. at 48.

4. The Arguments.

Dr. Jackson opines that taking Prozac caused Gilbert Rimbert to commit this homicide-suicide and that inadequate warnings in the Prozac labeling were the proximate cause of these events. See Plaintiff's Memorandum at 3, Exhibits A, B and C to Plaintiff's Memorandum, Report

at 50. Eli Lilly moves the Court to exclude Dr. Jackson's expert opinion testimony on general causation, specific causation, and proximate causation, on the grounds that she is not qualified to express such opinions, and she has not reliably applied her methodology to the facts. See Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. at 589-98; Norris v. Baxter Healthcare Corp., 397 F.3d 878, 883-84 (10th Cir. 2005). Eli Lilly argues that Dr. Jackson's opinions on general causation, specific causation, and proximate causation fail the tests for reliability and relevance that rule 702 of the Federal Rules of Evidence, and the Supreme Court's opinion in Daubert, require, and that the Court should exclude her opinions. See Motion at 1. Eli Lilly also contends that Dr. Jackson is not qualified to opine on the cause of homicide-suicide. See Motion at 3.

Eli Lilly maintains that Jackson "has shown herself to be an advocate, working exclusively for the law firm representing the plaintiff in this case, who formed conclusions about the case prior to study or review of available medical and scientific literature without knowing anything about the facts of this case." Id. at 5. Eli Lilly contends that Dr. Jackson's methodology was to "reach the desired conclusion first and then reason backward." Id. at 7. Eli Lilly maintains that "[s]uch a method is the antithesis of the scientific method and renders Jackson's opinions unreliable and inadmissible." Id.

Eli Lilly maintains that there are "insurmountable gaps" between the animal papers Dr. Jackson cites in her report, and Dr. Jackson's opinion that the same results would happen in humans and that, because of the results reported in animals about serotonin and dopamine levels, Prozac causes homicide-suicide. Motion at 12. Eli Lilly contends that Dr. Jackson's opinion fails the reliability requirement because she did not at least consider and account for existing epidemiological evidence that directly contradicts her general causation opinon on homicide-suicide.

Eli Lilly contends that Dr. Jackson's methodology first looks at the causal relationship, if

any, between Prozac and akathisia, second looks at the causal relationship, if any, between akathisia and homicide-suicide, and third implies from the first two steps, if proven, that Prozac must have had a causal relationship with homicide suicide -- "If A causes B and B causes C, then A must cause C." Motion at 16-17. Eli Lilly maintains that, because Jackson did not use the Hill criteria that "she personally embraces as the way to assess whether a suspected drug-adverse event relationship is causal" and because the Hill criteria is "the general causation methodology she testified is utilized by experts in the field," her methodology is unreliable and unhelpful to the trier of fact, and the Court should thus exclude her testimony. See Motion at 18.

Eli Lilly maintains that Dr. Jackson's use of the scientific method generated only untested hypotheses regarding causation, which do not provide a scientific basis to support a reliable expert opinion on general causation. See Motion at 19.

Mark Rimbert contends that Dr. Jackson is qualified to testify because she is a "board-certified psychiatrist" and an "assiduous researcher and writer." Plaintiff's Memorandum at 3. Mark Rimbert also argues that it is now "generally accepted" that SSRIs "trigger aggression and suicidality, inter alia, via drug-induced akathisia and psychosis." Id. at 2. Mark Rimbert supports this assertion by citing several peer-reviewed studies that Dr. Jackson did not include in her report. The first study was a small-scale study in which Dr. Anthony Rothschild "rechallenged"[3] three patients who had become akathisiatic and suicidal on Prozac again. Id. at 9. The phenomena replicated, and Dr. Rothschild noted that the negative effects were a result of the medication and were treatable. See Id (citing A.J. Rothschild & C. A. Locke, Re-exposure to Fluoxetine After Serious suicide attempts by Three Patients: The Role of Akathisia, 59 J. CLIN. PSYCHIATRY 491-93

[3] A rechallenge involves re-administering a drug after a first round of treatment has been terminated. This experiment allows an observer to test for a repeat reaction to a drug.

(1991)("Rothschild Study")).

A second study upon which Mark Rimbert relies is an epidemiological study which concludes that "people on Prozac were 6.6x more likely to commit acts of 'deliberate self-harm' than those on an older trycyclic antidepressant." Id. at 10 (citing S. Donovan, A. Clayton, M. Beeharry, S. Jones, C. Kirk, K. Waters, D. Gardner, J. Faulding & R. Madeley, Deliberate Self-harm and Antidepressant Drugs: Investigation of a Possible Link, 177 BRITISH J. PSYCH. 55-56 (2000) ("Donovan Article"). Rimbert also points to an epidemiological study which observed that "fluoxetine [the active ingredient in Prozac] has a rate [of suicidality] that is substantially higher than the other anti-depressants. Id (citing S. Jick, Antidepressants and Suicide, 310 BR. MED. J. 215-18 (1995)("Jick Article") . Finally, Mark Rimbert cites peer-reviewed meta-analyses that suggests that adults taking anti-depressants have a an increased risk of suicide attempts. Id. See I. Aursnes, I.F. Tvete, J. Gaasemyr & B. Natvig, Suicide Attempts in Clinical Trials with Peroxetine Randomized Against Placebo, 3 BMC MEDICINE 14 (2005)("Patients and doctors should be warned that the increased suicidal activity observed in children and adolescents taking certain antidepressant drugs may also be present in adults.")("Aursnes Article"); D. Fergusson, S. Doucette, K. C. Glass, S. Shapiro, D. Healy, P. Hebert & B. Hutton, The Association Between Suicide Attempts and SSRIs: A Systematic Review of Randomized Controlled Trials, 330 BMJ 396.

Mark Rimbert also maintains that Dr. Jackson's specific-causation analysis is sound because cases involving the adverse effects of drugs involve an interaction of multiple factors. Mark Rimbert argues that "it is highly inappropriate to suggest that the existence of one such factor. . . necessarily means that another factor was not 'substantial,' so as to rise to the level of 'proximate' cause." Id. 16.

The Court held a hearing on May 16, 2008, in which the parties argued their respective

positions regarding the admissibility of Dr. Jackson's testimony. See Transcript of May 16, 2008 Hearing at 85 (Doc. 103)("Tr."). At an earlier hearing, the Court told Mark Rimbert that it would not exclude Dr. Jackson or her testimony without giving her an opportunity to testify at the Daubert hearing. See Transcript of April 23, 2008, at 22 ("April 23 Tr.").[4] Mark Rimbert chose not to bring Dr. Jackson to testify, and the parties asked the Court to decide this motion on the briefing and attachments, and after oral argument. See id.

At the May 16, 2008 hearing, Mark Rimbert proffered an affidavit that Dr. Jackson prepared after submitting her report. See Tr. at 99:3 (Vickery). Eli Lilly objected, because the affidavit allegedly represented supplemental material that rule 26 would preclude as extraneous to the report. See id. at 99:8-14 (See). In any case, Mark Rimbert argued that Dr. Jackson's testimony would present more than mere possibilities, and that the "possibility-probability problem" arose only in the context of what the prescribing doctor would have done differently if an adequate warning had been in place. Tr. at 111 (Vickery). Eli Lilly contended that, under a valid special causation analysis, Dr. Jackson should be able to eliminate alternative causes to a "high degree of probability." Id. at 134 (See). The Court questioned Eli Lilly about allowing Dr. Jackson to testify about the same conclusions that underlie the FDA's warning label for Prozac. See id. at 151:8 (the Court). Eli Lilly argued that the FDA's label is based on conclusions that do not support, and in some parts contradict, Dr. Jackson's conclusion. See Tr. at 151:14 (See).

LAW REGARDING THE COURT'S DAUBERT ROLE

Since the Supreme Court decided Daubert v. Merrell Dow Pharmaceuticals, Inc., trial courts have had the responsibility to make certain that proffered experts will assist the jury in

[4] The Court's citations to the transcript of this hearing refer to the Court Reporter's original, unedited version. Any final transcript may contain slightly different page and/or line numbers.

understanding the evidence and in determining the factual issues it must decide. The Court must not only decide whether the expert is qualified to testify, but whether the opinion testimony is the product of a reliable methodology. Daubert requires the Court to scrutinize the proffered expert's reasoning to determine if that reasoning is sound.

1. Rule 702.

Rule 702 of the Federal Rules of Evidence governs the admissibility of expert testimony:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Fed. R. Evid. 702. Thus, rule 702 requires the trial court to "determine whether the expert is proposing to testify to (1) scientific, technical, or other specialized knowledge that (2) will assist the trier of fact to understand or determine a fact in issue." United States v. Muldrow, 19 F.3d 1332, 1337 (10th Cir. 1994). An expert is "required to possess such skill, experience or knowledge in that particular field as to make it appear that his opinion would rest on substantial foundation and would tend to aid the trier of fact in his search for truth." LifeWise Master Funding v. Telebank, 374 F.3d 917, 928 (10th Cir. 2004). The proponent of expert testimony has the burden of establishing that the pertinent admissibility requirements are met by a preponderance of the evidence. See Morales v. E.D. Etnyre & Co., 382 F.Supp.2d 1252, 1266 (D.N.M. 2005)(Browning, J.)(citing Bourjaily v. United States, 483 U.S. 171, 175 (1987)). Once the trial court has determined that expert testimony would be helpful to the trier of fact, a witness "may qualify as an expert by knowledge, skill, experience, training, or education and . . . the expert . . . should not be required to satisfy an overly narrow test of his own qualifications." Gardner v. Gen. Motors Corp., 507 F.2d 525, 528 (10th Cir.

1974)(internal quotation marks omitted). The Court should, under the Federal Rules of Evidence, liberally admit expert testimony, see United States v. Gomez, 67 F.3d 1515, 1526 (10th Cir. 1995)(describing rule 702 as a "liberal standard"), and the trial court has broad discretion in deciding whether to admit or exclude expert testimony, see Werth v. Makita Elec. Works, Ltd., 950 F.2d 643, 647 (10th Cir. 1991)(noting the trial court's decision will not be overturned "unless it is manifestly erroneous or an abuse of discretion").

2. The Daubert Standard.

In its role of gatekeeper, the Court must assess the reasoning and methodology underlying an expert's opinion and determine whether it is both scientifically valid and relevant to the facts of the case, i.e., whether it is helpful to the trier of fact. See Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. at 594-95; Witherspoon v. Navajo Refining Co., LP, No. CIV 03-1160 BB/LAM, 2005 WL 5988649 at *2 (D.N.M. July 18, 2005)(Black, J.)(citing Dodge v. Cotter Corp., 328 F.3d 1212, 1221 (10th Cir. 2003)). The Supreme Court articulated a non-exclusive list of factors which weigh into a district court's first-step reliability determination, including: (i) whether the method has been tested; (ii) whether the method has been published and subject to peer review; (iii) the error rate; (iv) the existence of standards and whether the witness applied them in the present case; and (v) whether the witness' method is generally accepted as reliable in the relevant medical and scientific community. See Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 594-95. The court is also to consider whether the witness' conclusion represents an "unfounded extrapolation" from the data; whether the witness has adequately accounted for alternative explanations for the effect at issue; whether the opinion was reached for the purposes of litigation or as the result of independent studies; or whether it unduly relies on anecdotal evidence. See Witherspoon v. Navajo Refining Co., LP, 2005 WL 5988649 at *3 (citing Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)). The United

States Court of Appeals for the Tenth Circuit stated the applicable standard in Norris v. Baxter Healthcare Corp.:

> Rule 702 requires the district court to "ensure that any and all scientific testimony or evidence is not only relevant, but reliable." Id. [Bitler v. A.O. Smith Corp., 391 F.3d 1114, 1120 (10th Cir. 2004)](quoting Daubert, 509 U.S. at 589, 113 S.Ct. 2786). This obligation involves a two-part inquiry. Id. "[A] district court must [first] determine if the expert's proffered testimony . . . has 'a reliable basis in the knowledge and experience of his [or her] discipline.' " Id. (quoting Daubert, 509 U.S. at 592, 113 S.Ct. 2786). In making this determination, the district court must decide "whether the reasoning or methodology underlying the testimony is scientifically valid. . . ." Id. (quoting Daubert, 509 U.S. at 592-93, 113 S.Ct. 2786). Second, the district court must further inquire into whether proposed testimony is sufficiently "relevant to the task at hand." Daubert, 509 U.S. at 597, 113 S.Ct. 2786.

397 F.3d at 883-84 (footnote omitted). "The second inquiry is related to the first. Under the relevance prong of the Daubert analysis, the court must ensure that the proposed expert testimony logically advances a material aspect of the case. . . . The evidence must have a valid scientific connection to the disputed facts in the case." Norris v. Baxter Healthcare Corp., 397 F.3d at 884 n.2 (citing Daubert v. Merrell Dow Pharm., Inc., 43 F.3d 1311, 1315 (9th Cir. 1995) (on remand) and Daubert v. Merrell Dow Pharm., Inc., 509 U.S. at 591)). If the expert's proffered testimony fails on the first prong, the court does not reach the second prong. See Norris v. Baxter Healthcare Corp., 397 F.3d at 884.

In conducting its Daubert review, the court must focus generally on "principles and methodologies, and not on the conclusions generated." Armeanu v. Bridgestone/Firestone N. Am., Tire, LLC, No. CIV 05-0619 JB/DJS, 2006 WL 4060665 at *11 (D.N.M.)(Browning, J.)(citing Daubert v. Merrell Dow Pharm., Inc., 509 U.S. at 595). "Despite this focus on methodology, 'an expert's conclusions are not immune from scrutiny . . . and the court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." Armeanu v. Bridgestone/Firestone N. Am., Tire, LLC, 2006 WL 4060665 at * 11 (internal quotation marks and

bracket omitted). The proponent of the expert's opinion testimony bears the burden of establishing that the expert is qualified, that the methodology he or she uses to support his or her opinions is reliable, and that his or her opinion fits the facts of the case and thus will be helpful to the jury. See Norris v. Baxter Healthcare Corp., 397 F.3d at 881. As the Tenth Circuit noted in Hollander v. Sandoz Pharmaceuticals Corp., 289 F.3d 1193 (10th Cir. 2002):

> Because the district court has discretion to consider a variety of factors in assessing reliability under Daubert, and because, in light of that discretion, there is not an extensive body of appellate case law defining the criteria for assessing scientific reliability, we are limited to determining whether the district court's application of the Daubert manifests a clear error of judgment or exceeds the bounds of permissible choice in the circumstances. . . . Thus, when coupled with this deferential standard of review, Daubert's effort to safeguard the reliability of science in the courtroom may produce a counter-intuitive effect: different courts relying on the essentially the same science may reach different results.

289 F.3d at 1206. As the United States Court of Appeals for the Ninth Circuit noted in Claar v. Burlington Northern Railroad Co., 29 F.3d 499 (9th Cir. 1994):

> Coming to a firm conclusion first and then doing research to support it is the antithesis of this method. Certainly, scientists may form initial tentative hypotheses. However, scientists whose conviction about the ultimate conclusion of their research is so firm that they are willing to aver under oath that it is correct prior to performing the necessary validating tests could properly be viewed by the district court as lacking the objectivity that is the hallmark of the scientific method.

29 F.3d at 502-503.

"Once reliability is established, however, it is still within the district court's discretion to determine whether expert testimony will be helpful to the trier of fact. In making that determination, the court should consider, among other factors, the testimony's relevance, the jurors' common knowledge and experience, and whether the expert's testimony may usurp the jury's primary role as the evaluator of evidence." Ram v. N.M. Dep't of Environment, No. CIV 05-1083 JB/WPL, 2006 WL 4079623 at * 10 (citing United States v. Rodriguez-Felix, 450 F.3d 1117, 1123 (10th Cir.

2006)).

An expert may not rely on materials not identified in his or her rule 26 report, and his or her opinions are not admissible if not described in the report. See Fed. R. Civ. P. 26(a)(2)(B)(summarizing the requirements for expert reports). Rule 26 of the Federal Rules of Civil Procedure provides:

> Written Report. Unless otherwise stipulated or ordered by the court, this disclosure must be accompanied by a written report--prepared and signed by the witness--if the witness is one retained or specially employed to provide expert testimony in the case or one whose duties as the party's employee regularly involve giving expert testimony. The report must contain:
>
> (i) a complete statement of all opinions the witness will express and the basis and reasons for them;
>
> (ii) the data or other information considered by the witness in forming them;
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> (iii) any exhibits that will be used to summarize or support them;
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> (iv) the witness's qualifications, including a list of all publications authored in the previous 10 years;
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> (v) a list of all other cases in which, during the previous four years, the witness testified as an expert at trial or by deposition; and
>
> (vi) a statement of the compensation to be paid for the study and testimony in the case.

Fed. R. Civ. P. 26(a)(2)(B). An expert witness is not permitted to express opinions beyond the materials identified in his or her report. See In re Breast Implant Litigation, 11 F.Supp.2d at 1233 n.4; Morales v. E.D. Entyre & Co., 382 F.Supp.2d at 1267 (disregarding opinion that was not disclosed in the expert's report).

An untested hypothesis does not provide a scientific basis to support an expert opinion. See Norris v. Baxter Healthcare Corp., 397 F.3d at 887 ("[A]t best, silicone-associated connective tissue disease is an untested hypothesis. At worst, the link has been tested and found to be untenable.

Therefore, there is no scientific basis for any expert testimony as to its specific presence in Plaintiff."); In re Breast Implant Litigation, 11 F.Supp.2d at 1228 ("An untested hypothesis cannot be a scientifically reliable basis for an opinion on causation."). A court is not required "to admit opinion evidence that is connected to existing data only by the ipse dixit of the expert. The court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997). See Hollander v. Sandoz Pharm. Corp., 289 F.3d 1193, 1209 (10th Cir. 2002)(lack of similarity between animal studies and human studies, including dose and route administration); Tyler v. Sterling Drug., Inc., 19 F.Supp.2d 1239, 1244 (N.D. Okla. 1998)("Test results on animals not necessarily reliable evidence of the same reaction in humans.").

Epidemiological studies are the best evidence of causation in a toxic tort case, like this one, in which exposure to a substance is alleged to have caused injury. See Norris v. Baxter Healthcare Corp., 397 F.3d at 882 ("[E]pidemiology is the best evidence of general causation in a toxic tort case."); See In re Breast Implant Litigation, 11 F.Supp.2d at 1224 ("Epidemiology is the best evidence of causation in the mass torts context."). In such cases, a "lack of epidemiologic studies supporting a plaintiff's claim creates a high bar for a plaintiff to surmount with respect to the reliability requirement." Faris v. Intel Corp., 493 F.Supp.2d 1174, 1181 (D.N.M. 2007)(Black, J.)(internal quotation marks and brackets omitted). "[W]here there is a large body of contrary epidemiologic evidence, it is necessary to at least address it with evidence that is based on medically reliable and scientifically valid methodology." Norris v. Baxter Healthcare Corp., 397 F.3d at 882. "While the presence of epidemiology does not necessarily end the inquiry, where epidemiology is available, it cannot be ignored. As the best evidence of general causation, it must be addressed." Id. "Non-epidemiology studies, singly or in combination, are not capable of proving causation in

human beings in the face of an overwhelming body of contradictory epidemiology evidence." Id. at 887 n.6 (internal quotation marks and brackets omitted).

Indirect, chain-of-events causation was not a generally-accepted scientific methodology in Miller v. Pfizer, Inc., 196 F.Supp.2d 1062 (D.Kan. 2002), aff'd, 356 F.3d 1326 (10th Cir. 2004). In Miller v. Pfizer, Inc., the plaintiffs alleged that their thirteen-year-old son committed suicide because he took Zoloft, an SSRI. See id. at 1064. The plaintiffs' expert, Healy, relied heavily on case reports and his own studies and calculations, and disavowed the need for randomized controlled trials and epidemiological studies. See id. at 1067. Healy also relied on two studies on treatment with fluoxetine. See id. at 1070-71. The district court noted that "large-scale epidemiological studies are not essential to the formation of an expert opinion as to causation" Id. at 1072. The district court further noted that the "general acceptance" factor "bears on the technique used . . . rather than the conclusion reached." Id. at 1075. The district court concluded:

> generally accepted methodology . . . required Dr. Healy to consistently test the strength of association between SSRI drugs and suicide (the outcome of interest) -- rather than the association between SSRI drugs and and akathisia (which is purported to be part of the chain of events that lead to suicide, rather than an independent outcome."

Id. at 1080.

Courts have excluded experts' opinions when the experts depart from their own established standards. See Truck Ins. Exchange v. Magnetek, Inc., 360 F.3d at 1213 ("The district court noted that [the expert]'s opinion did not meet the standards of fire investigation [the expert] himself professed he adhered to."); Magdaleno v. Burlington Northern R. Co., 5 F.Supp.2d 899, 905 (D.Colo. 1998)("In sum, [the expert]'s methodology is not consistent with the methodologies described by the authors and experts whom [the expert] identifies as key authorities in his field.").

In Hollander v. Sandoz Pharamceutical Corp., the United States District Court for the West

District of Oklahoma excluded expert testimony where the expert "could only list 'possible' mechanisms" that a drug caused certain injuries. 95 F.Supp.2d 1230, 1235 (W.D. Okla 2000), aff'd in part, 289 F.3d 1193 (10th Cir. 2002). The expert admitted that his opinion on the mechanism or potential effect of the drug at issue "was still only a hypothesis, as opposed to scientific knowledge." Id. at 1236.

The expert opinions at issue in Hollander v. Sandoz Pharmaceutical Corp. involved whether the drug Parlodel caused hypertension. The excluded testimony comprised uncontrolled and anecdotal case reports, animal studies only tangentially related to the substance at issue in the case, and a hypothesis that Parlodel might behave like substances from the same class, which cause hypertension. Id. at 1235. The district court in Hollander v. Sandoz Pharmaceutical Corp. concluded:

> [D]ue to the absence of supportive epidemiological evidence, the differences between bromocriptine [the substance underlying Parlodel] and the other ergot alkaloids, the dissimilarity of the animal studies, and the unreliability of the case reports, the data and methods relied on by the plaintiffs' experts do not furnish a scientifically valid basis for their conclusion that Parlodel causes strokes.

Id. at 1239. The Tenth Circuit affirmed the district court in excluding the testimony. See Hollander v. Sandoz Pharmaceutical Corp., 289 F.3d at 1207("Accordingly, the district court did not abuse its discretion in finding that bromocriptine's similarity to other ergot alkaloids constituted an unreliable basis on which to conclude that the drug causes vasoconstriction and ensuing adverse effects like Ms. Hollander's stroke.").

ANALYSIS

Eli Lilly maintains that the Court should exclude Dr. Jackson's testimony. Eli Lilly argues that Dr. Jackson is not qualified, and that her proposed testimony does not meet the standards of reliability and relevance that Daubert requires. The Court disagrees, and finds that Dr. Jackson is

qualified, and that her testimony is admissible.

I. DR. JACKSON IS QUALIFIED TO TESTIFY IN THIS CASE.

Mark Rimbert has challenged Dr. Jackson's qualifications for testifying in this case. The main basis for the challenge is that Dr. Jackson does not have expertise in the discrete literature of "Homicide-suicide." The Court finds that a lack of familiarity with a subset of the general phenomenon about which Dr. Jackson seeks to testify does not disqualify her.

Dr. Jackson is a board-certified psychiatrist who has treated mental illness and prescribed anti-depressants. She is therefore qualified to testify about the possible harmful effects of medication. Moreover, as Dr. Jackson notes in her Affidavit, "the reification of [the concept of "homicide-suicide] by an esoteric community of researchers should not be allowed to impeach the credibility of other professionals who have chosen to employ a different terminology . . . or a different emphasis for the same events." Jackson Aff. at 2.

One other basis upon which Mark Rimbert challenges Dr. Jackson's qualifications is the fact that she is not an expert at writing warning labels. The Court does not believe that a medical doctor testifying about the effect that the contents of a warning label might have requires expertise in writing labels. The pertinent expertise is in psychiatry, in the medications at issue in this case, and in the effects those medications have on individuals. Accordingly, the Court finds that Dr. Jackson is qualified to testify in this case. Moreover, the Court will admit her testimony because, according to the standard of Daubert v. Merrell Dow Pharmaceuticals, Inc., the methodology upon which she bases her opinion is reliable.

II. THE COURT WILL NOT ENTIRELY DISREGARD THE MATERIALS ATTACHED TO THE RESPONSE.

Eli Lilly argues that the Court should not consider the materials Mark Rimbert provided as

attachments to the Response or the Affidavit of Grace E. Jackson, M.D., because those materials are supplemental to the report. The Court is mindful of the risk of unfairness to Eli Lilly that can result from looking beyond the expert report, and from allowing the expert to bolster or expand the bases for her testimony after submitting her report. The Court will not allow Dr. Jackson to expand the scope of her opinion. At the same time, the Court will consider the extra material to the extent that it clarifies what is already in the report. See Tr. at 114: 4 (the Court). Moreover, the Court can properly look to materials on which Dr. Jackson may not rely to determine whether the studies on which she relied are peer-reviewed and themselves reliable; whether the method in the studies has been tested; whether standards exist, and whether Dr. Jackson applied them in this case; and whether Dr. Jackson's methodology is generally accepted and reliable.

III. DR. JACKSON APPLIED A RELIABLE METHODOLOGY.

Under Daubert v. Merrell Dow Pharmaceuticals, Inc., a court must determine whether proffered expert testimony will be helpful to the jury. See 509 U.S. at 592 ("Faced with a proffer of expert scientific testimony, then, the trial judge must determine at the outset, pursuant to Rule 104(a), whether the expert is proposing to testify to (1) scientific knowledge that (2) will assist the trier of fact to understand or determine a fact in issue."). Although the Court recognizes some of the flaws that Eli Lilly has pointed out in Dr. Jackson's methodology, the Court ultimately finds that Dr. Jackson based her methodology on reliable data to support her conclusions. After reviewing Dr. Jackson's report, the Court determines that her methodology lends her testimony sufficient indicia of reliability. Specifically, the methodology relies on peer-reviewed, scientific studies, and valid inferences based on those studies. Her opinions therefore qualify for admissibility under the Daubert standard.

A. THERE ARE SIGNIFICANT WEAKNESSES IN DR. JACKSON'S METHODOLOGY.

Eli Lilly makes multiple attacks on Dr. Jackson's methodology. One of the challenges that Eli Lilly raises is that Dr. Jackson did not follow a scientific approach to her investigation. They support this allegation by citing an e-mail exchange that occurred when Dr. Jackson first learned about this case.

Dr. Jackson first learned of this case in an e-mail from Mr. Vickery's office, which states:

> Grace:
>
> Pros: It's a murder-suicide. Man was on Prozac, shot his wife, his dog and then himself. Need report.
>
> Cons: Report due 9/24/07.
>
> Are you up for it?

Exhibit C to Motion, E-mail from Karin Shepherd, Secretary to Mr. Vickery, to Jackson regarding Rimbert v. Eli Lilly (dated September 5, 2007)("September 5, 2007 e-mail"); Jackson Depo. at 271:9-272:12. Approximately six hours later, knowing nothing about the case other than the information she received in the September 5, 2007 e-mail, Dr. Jackson responded: "That sounds like an EXCELLENT case." Exhibit D to Motion, E-mail from Dr. Jackson to Shepherd (dated September 5, 2007)("Response to September 5, 2007 e-mail"); Jackson Depo. at 272:13-15; id. at 273:18-275:12.

Dr. Jackson is aware that there is a body of published medical literature regarding homicide-suicide, but she has not studied that literature. See Jackson Depo.at 60:17-61:15; id. at 139:13-18. Other than "skimming abstracts," Dr. Jackson did not read any articles on homicide-suicide while formulating her causation opinions in this case because of "time constraints in the production of her report." Id. at 60:17-61:15. Dr. Jackson does not know whether the recognized risk factors for

homicide-suicide are the same as those for an isolated homicide, about the different types of homicide-suicide, or whether there are different risk factors for different types of homicide-suicide. See id. at 139:2-12; id. at 140:3-17. Specifically, Dr. Jackson cannot opine about the relevance of a history of prior violence or domestic violence as a risk factor for different types of homicide-suicide, because she has not researched these issues in the medical literature. See id. at 141:2-11.

Dr. Jackson testified that experts in the area of epidemiology and pharmacovigilance use the criteria of Sir Austin Bradford Hill to assess whether a drug causes a specific adverse event. See Second Jackson Depo. at 76:22-77:5, id. at 77:15-25. Eli Lilly contends that, in Hill's article The Environment and Disease: Association or Causation? 58 Proceedings Royal Society Medicine (1965), Hill states:

> After a statistically significant association is shown, factors to be considered in causation analysis include: 1) strength of association, 2) consistency of the association, 3) specificity of the association, 4) temporal relation between exposure and the adverse event, 5) biological gradient (dose-response relationship), 6) biological plausibility, 7) coherent with generally known facts about the disease, 8) experimental results, and 9) analogy.

Id. at 295-300 (quoted in Memo. in Support of Motion to Exclude at 17 n.15). Dr. Jackson did not use the Hill criteria in formulating her general causation opinion in this case regarding whether Prozac can cause homicide-suicide. See Jackson Depo. at 155:8-14.

Dr. Jackson testified that she followed the general scientific method in formulating her opinions in this case, consisting of five steps: (i) generating a hypothesis; (ii) formulating a plan of investigation or protocol regarding the procedure for data gathering and data analysis; (iii) gathering data following the protocol procedures; (iv) analyzing the data using methods set forth in the protocol; and (v) comparing results from the data analysis with the hypothesis to see whether the hypothesis was proven or disproven. See Jackson Depo. at 156:25-158:8, id. at 158:17-19. Dr.

Jackson testified that many articles on which she relies for her general causation opinion cannot support a valid scientific conclusion and are capable, at most, of generating hypotheses on the issue of general causation. See Jackson Depo. at 195:7-20, id. at 201:17-202:10, id. at 266:23-269:6. In her report, Dr. Jackson opines: "Human studies have consistently demonstrated an association between low levels of 5HIAA in the spinal fluid, and impulsivity, aggression, and suicide." Report at 44. From that observation, Dr. Jackson extrapolates that the fact that Prozac induces this type of metabolic disturbance "suggests the existence of an inherent destabilizing effect." Id.

Dr. Jackson cites all the medical and scientific data upon which she relied in her report. See Jackson Depo. at 18:19-19:1; id. at 30:6-11; id. at 36:22-37:5. Dr. Jackson does not, however, cite medical literature on homicide-suicide in her report. See Jackson Depo. at 61:12-15. Jackson cites two Prozac studies in humans. The data reported in the Cusin and Perlis articles, however is uncontrolled. This means that there is no "placebo control arm" – or group not taking Prozac – to compare to the group of patients who are taking Prozac. Jackson Depo. at 183:25-184:22; id. at 196:2-7. The authors of the Cusin and Perlis articles recognize the limitations inherent in their studies because of the lack of control groups. See Cusin article at 56 ("The major limitations of the present study are the post hoc nature of the analyses and the absence of a placebo double-blind control."); Perlis article at 45 ("A second limitation in the present study is the absence of a placebo or active comparator group.").

The lack of a control group makes it difficult to state whether the adverse events observed were a result of fluoxetine, part of the natural history and fluctuations of depression, or caused by other factors. See Cusin article at 55 ("Worsening may have different possible explanations. For example, worsenings during the first few weeks of treatment may not be etiologically related to antidepressant therapy, but may simply represent a correlate of the natural history of the disease.");

id. ("Worsening may be a secondary to stressful life events. . . ."); Perlis article at 45 ("It is thus impossible to establish a specific association between fluoxetine and treatment-emergent adverse events."); Jackson Depo. at 185:24-186:5; id. at 197:12-198:3. Dr. Jackson agrees that, because there was no control group in either study, one cannot draw a scientifically valid conclusion, from either paper, that Prozac caused or was even associated with the observed adverse events reported, whether worsening of depression in the Cusin article or suicidal thinking in the Perlis article. See Jackson Depo. at 195:7-20; id. at 201:17-202:10.

Suicide, homicide, and homicide-suicide occur in the general population, specifically in individuals who are not taking Prozac or any other antidepressant. See Exhibit H to Mem. in Support of Motion to Exclude, Declaration of Kenneth Tardiff, M.D., ¶ 2, at 2 (taken March 11, 2008)("Tardiff Aff."). Without controlled data, there is no way to know whether such events are more common in depressed patients taking Prozac than in depresssed patients not taking Prozac or any antidepressant drug. See In re Breast Implant Litigation, 11 F.Supp.2d at 1224 ("Without a controlled study, there is no way to determine if those symptoms are more common in women with silicone breast implants than women without implants."); Reference Manual on Scientific Evidence at 95 (Federal Judicial Education Center 2d ed. 2000)("Was there a control group? If not, the study has little to say about causation.").

1. Animal Studies.

Dr. Jackson also relies on several studies conducted on animals – namely, monkeys and rats. See Report at 51-52 (references numbered 31 and 36-39). Dr. Jackson contends that the cited animal studies demonstrate that Prozac reduced the level and activity of neurotransmitteres in the brain, serotonin and dopamine, "believed to account for akathisia and other side effects which can lead to aggression and suicide." Id. at 46.

Two of the animal papers that Dr. Jackson represents to be studies of Prozac in rat brains did not study Prozac at all. See Exhibit I to Memo. in Support of Motion to Exclude (reference 36 in Jackson's Report), M. Di Mascio, G. Di Giovanni, V. Di Matteo, S. Prisco, & E. Esposito, Selective Serotonin Reuptake Inhibitors Reduce the Spontaneous Activity of Dopaminergic Neurons in the Ventral Tegmental Area, 46:6 Brain Research Bulletin 547-54 (1998); Exhibit J to Memo. in Support of Motion to Exclude (reference 37 in Jackson's Report), F. Yamane, H. Okazawa, P. Blier, & M. Diksic, Reduction in Serotonin Synthesis Following Acute and Chronic Treatments With Paroxetine, a Selective Serotonin Reuptake Inhibitor, In Rat Brain: An autoradiographic study with alpha-[14C]Methyl-l-tryptophan, 62 J. Biochemical Pharmacology 1481-89 (2001). Dr. Jackson admits that her report is in error on that point. See Jackson Depo. at 317:3-6, 319:11-25. Another animal paper cited by Dr. Jackson is a study of the effect of chronic administration of Prozac on the brains of monkeys, and reports the opposite of Dr. Jackson's contention that Prozac reduces the level and activity of neutrotransmitters , seotonin, and dopamine in the brains of monkeys. See Exhibit K to Memo. in Support of Motion to Exclude (reference 31 in Jackson's report), T. Smith, R. Kuszenski, K. George-Friedman, J.D. Malley, & S.L. Foote, In Vivo Microdialysis Assessment of Extracellular Serotonin and Dopamine Levels in Awake Monkeys During Sustained Fluoxetine Admininstration, 38 Synapse 460-70 (2000), Second Jackson Depo. at 331:18-21, 333:15-25.

Dr. Jackson concedes that there are substantial differences between the brains of animals – both rodent and primate – and the brains of human beings in response to administration of antidepressants. See Second Jackson Depo. at 323:14-21. Dr. Jackson performed no calculations to determine whether the dose or route of administration of antidepressants to rats and monkeys in the papers that she cited in her report was equivalent or substantially similar to human beings taking prescribed doses of Prozac. See Jackson Depo. at 322:13-23. Dr. Jackson agrees that the animal

studies that she cited in her report create hypotheses about what might happen in humans. See Jackson Depo. at 266:23-267:6; id. at 269:10-270:3; Second Jackson Depo. at 324:13-16. Any of the effects discussed in the animal papers cited by Dr. Jackson remain unproven because the testing methodologies used by the authors of those papers have not or cannot be conducted on humans with present technology. See Jackson Depo. at 268:3-14-270:3; Second Jackson Depo. at 325:1-20.

2. Epidemiological Evidence.

Dr. Jackson's report does not contain any citation to, and she does not rely on, any controlled clinical trial or other epidemiological study which demonstrates that the ingestion of Prozac creates an increased risk or an increased incidence of the following conditions: akathisia, suicidal thinking, suicidal behavior or completed suicide, violence or homicidal behavior, worsening depression, psychotic decompensation, psychiatric rage, impulsivity or impulsive behavior, or disinhibition or diminished capacity to resist engaging in homicidal or suicidal behavior. See Jackson Depo. at 163:24-166:9; id. at 170:14-171:13; id. at 173:24-174:24; id. at 250:7-14; id. at 251:7-11. A controlled clinical trial is an epidemiological study which "is considered the gold standard for determining the relationship of an agent to a disease or health outcome." Reference Manual on Scientific Evidence, supra, 338.

Dr. Jackson is aware of a body of published medical and scientific literature, including controlled clinical trials and other epidemiological studies, which supports the proposition that Prozac is not associated with suicidality, but she did not read or consider that literature in the formations of her opinions and report in this case. See Jackson Depo. at 66:11-21. Dr. Jackson is aware that the FDA reported to the public and to medical communities the results of its analysis of controlled clinical trials of antidepressants, including Prozac, and its conclusions that ingestion of antidepressants, including Prozac, create no increased risk of suicidality in adults over twenty-four

years of age and there is a decreased risk of suicide in individuals over the age of sixty-five years old. See id. at 174:25-177:9. Dr. Jackson does not dispute the FDA's interpretation of that data, but she has not analyzed the data set herself. See id. at 175:10-177:9. Dr. Jackson is aware that there are available controlled clinical trial data that examine the issue whether Prozac caused suicide, but she has not looked at that data. See id. at 177:4-9; id. at 203:10-15.

There are published controlled clinical trials, meta-analyses of controlled clinical trials, and other epidemiology studies which support the proposition that Prozac and other SSRIs or other antidepressants are not associated with suicidality or violent, aggressive behavior. See Exhibit N to Motion, Plewes Decl.; Exhibit 1 to Plewes Decl., Bibliography listing articles regarding meta-analyses of controlled clinical trials with fluoxetine, SSRIs, and antidepressants.[5] There is also a

[5] C. Beasley et al., Fluoxetine and Adult Suicidality Revisited, an Updated Meta-Analysis Using Expanded Data Sources From Placebo-Controlled Trials, 27:6 J. Clinical Psychopharmacology 682-86 (2007)(concluding that there were no statisically significant Mantel-Henszel Risk Difference between patients treated with fluoxetine and those treated with placebo); S. Tauscher-Wisniewski, D. Disch, J. Plewes, S. Ball, & C. Beasley, Evaluating Suicide-Related Adverse Events in Clinical Trials of Fluoxetine Treatment in Adults for Indications Other than Major Depressive Disorder, 37 Psychological Medicine 1585-93 (2007)(concluding "[t]he risk of treatment-emergent suicidality does not appear to be associated with fluxotine treatment for adults with various non-MMD conditions"); D. Gunnell, J. Saperia, & D. Ashby, Selective Serotonin Reuptake Inhibitors (SSRIs) and Suicide in Adults: Meta-Analysis of Drug Company Data from Placebo Controlled, Randomised Controlled Trials Submitted to the MHRA's Safety Review, 330 BMJ 1-5 (2005)(finding "it is possible, in the early weeks of treatment, that SSRIs are associated with an increased risk of suicidal behavior."); G. Tollesfson et al., Absence of Emergent Suicidal Ideation During Treatment: A Comparative, Controlled, Double-Blind Analysis Employing Several Distinct Antidepressants, 2 Depression 73-79 (1994); G. Tollefson, Absence of a Relationship Between Adverse Events and Suicidality During Pharacotherapy for Depression 14:3 J. Clinical Psychopharmacology 163-69 (1994); D. Goldstein and C. Beasley et al., Analyses of Suicidality in Double-Blind, Placebo-Controlled Trials of Pharmacotherapy for Weight Reduction, 54:8 J. Clinical Psychiatry 309-316 (1993); Beasley et al., Fluoxetine: no association with suicidality in obsessive-compulsive disorder, 24 J. Affective Disorders 1-10 (1992); D. Wheadon, Lack of Association between fluoxetine and suicidality in bulimia nervosa, 53 J. Clinical Psychiatry 235-41 (1992). C. Beasley et al., Fluoxetine and suicide: a meta-analyses of controlled trials of treatment for depression 303 BMJ 685-91 (1991)(stating that "[s]uicidal acts did not differ significantly in comparisons of fluoxetine with placebo"); G. Tollesfson et al., Does Pharmacotherapy Induce

significant number of epidemiological studies in the published medical literature that treat homicide-suicide as a discrete subject. See Tardiff Aff.[6] Jackson admits that, because of her lack of

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Paradoxical Worsening in Some Patients?, 1 Depression 105-107 (1993)(concluding "[p]aradoxical worsening occurred infrequently in patients with major depression treated with fluoxetine" compared with those treated with "placebo" or "tricyclics").

[6] S. Salari, Patterns of Intimate Partner Homicide Suicide in Later Life: Strategies for Prevention, 2(3) Clinical Interventions in Aging 441-52 (2007); R. Bossarte, T. Simon & L. Barker, Characteristics of Homicide Followed by Suicide Incidents in Multiple States, 2003-04, 12 Injury Prevention 1133-38 (2006)("Approximately one quarter of homicide/suicide incidents involve persons over the age of 55."); M. Dawson, Intimate Femicide Followed by Suicide: Examining the Role of Premeditation, 31(1) Suicide and Life-Threatening Behavior 76-90 (2005); R. Comstock et al., Epidemiology of Homicide-Suicide Events, Oklahoma, 1994-2001, 26:3 Am. J. Forensic Medicine and Pathology 229-35 (2005); J. Malphurs & D. Cohen, A State-wide Case-Control Study of Spousal Homicide-Suicide in Older Persons, 13:3 Am. J. Geriatric Psychiatry 211-17 (2005)(concluding that sixty-five percent of homicide-suicide perpetrators were reported to have a depressed mood before their death and that only one suicide control subject tested positive for antidepressants); B. Barraclough & E. Harris, Suicide Preceded by Murder; The Epidemiology of Homicide-Suicide in England and Wales 1988-92, 32 Psychological Medicine 577-84 (2002)(concluding "[h]omicide-suicide in England and Wales is mostly a 'family matter,' men of predominately lower social class killing their kin, and pre-menopausal mothers their young children, before they kill themselves."); J. Malphurs & D. Cohen, A Newspaper Surveillance Study of Homicide-Suicide in the United States, 23(2) Am. J. Forensic Medicine and Pathology 142-48 (2002); C. Campanelli & T. Gilson, Murder-Suicide in New Hampshire, 1995-2000, 23(3) Am. J. Forensic Medicine and Pathology 248-51 (2002)(noting that, out of the sixteen cases identified in the study, eleven involved a spouse or consortial relationship between victim and assailant, and males were ninety-four percent of the perpetrators and females were eighty-eight percent of the victims); A. Felthous et al., 46(3) Combined Homicide-Suicide in Galveston County 586-92 (2001); L. Lund & S. Smorodinsky, Violent Death Among Intimate Partners: A Comparison of Homicide and Homicide Followed By Suicide in California, 31(4) Suicide and Life Threatening Behavior 451-59 (2001); D. Cohen, M. Llorente & C. Eisdorfer, Homicide-Suicide in Older Persons 155:3 Am. J. Psychiatry 390-96 (1998)(hypothesizing that the rate of homicide-suicide is increasing in the older population, and that the high rates of homicide-suicide in older Florida couples may be a result of the "lethal combination of depression and hopelessness in male caregivers."); D. Lecomte & P. Fornes, Homicide Followed by Suicide: Paris and its Suburbs 1991-1996, 43 J. Forensic Science 760-64 (1998); E. Morton et al., Partner Homicide-Suicide Involving Female Homicide Victims: A Population-Based Study in North Carolina, 1988-1992, 13:2 Violence and Victims 91-106 (1998); Y. Aderibigbe, Violence in America: A Survey of Suicide Linked to Homicides 42 J. Forensic Science 662-65 (1997)(concluding that "[s]pousal or consortial murder-suicide was the predominant type in each of the year under review, except for 1991 where familicide-suicide was the predominant type of murder-suicide."); C. Milroy, M. Dratsas, & D. Ranson, Homicide-Suicide in Victoria, Australia, 18(4) Am. J. of Forensic Medicine and Pathology 369-73 (1997); A. Felthous & A.

familiarity with the homicide-suicide literature, she does not know the recognized risk factors for a stand-alone homicide. See Jackson Depo. at 139:2-18, id. at 140:3-17; id. at 141:2-11. Dr. Jackson failed to consider, and in the case of homicide-suicide knowingly disregarded, essentially all of the published medical and scientific literature on causation. Dr. Jackson admits that she has not attempted to publish, in any peer-reviewed journal, the general causation method she used to generate her opinion that Prozac can cause homicide-suicide. Dr. Jackson also concedes that she has not sought to have her methodology peer reviewed by any other means, such as presenting her methodology at a scientific meeting. See Jackson Depo. at 55:17-56:3. Dr. Jackson also admits that she has not tested her general causation methodology to assess whether the methodology produces accurate results. See Third Jackson Depo. at 337-38.

The FDA's label insert for Prozac also relies on epidemiological evidence. The label states:

> Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder and other psychiatric disorders. Anyone considering the use of Prozac or any other antidepressant in a child, adolescent, or young adult, must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain psychiatric disorders are themselves associated with increases in the risk of suicide.

Hempel, Combined Homicide-Suicides: A Review, 40 J. Forensic Science 846-857 (1995); C. Milroy, Reasons for Homicide and Suicide in Episodes of Dyadic Death in Yorkshire and Humberside, 35:3 Medical Science Law 213-17 (1995); P. Marzuk, K. Tardiff, & C. Hirsch, The Epidemiology of Murder-Suicide, 267:23 JAMA 3179-83 (1992); M. Rosenbaum, The Role of Depression in Couples Involved in Murder-Suicide and Homicide, 147:8 Am. J. Psychiatry 1036-1039 (1990); A. Copeland, Dyadic Death – Revisited, 25 J. Forensic Science Society 181-88 (1985); N. Allen, Homicide Followed By Suicide: Los Angeles, 1970-1979, 13(3) Suicide and Life-Threatening Behavior 155-165 (1983)("Murder-suicide offenders are older men who seem to be a less deviant group than the typical murderers."); A. Berman, Dyadic Death: Murder-Suicide, 9(1) Suicide and Life-Threatening Behavior 15-23 (1979); M. Wolfgang, An Analysis of Homicide-Suicide, 6:3 J. Clinical and Experimental Psychopathology 208-18 (1958).

Exhibit BB to Plaintiff's Memorandum in Opposition to Defendant's Motion to Exclude Dr. Grace Jackson at 1, filed April 17, 2008 (Doc. 75)("FDA Warning").

B. THE DAUBERT FACTORS WEIGH IN FAVOR OF ADMITTING DR. JACKSON'S TESTIMONY.

In assessing whether an expert's testimony is reliable and will assist the jury, a court must examine the expert's proposed methodology in light of the non-exclusive set of factors that the Supreme Court of the United States enumerated in Daubert v. Merrell Dow Pharmaceuticals, Inc. Those factors include (i) whether the method has been tested; (ii) whether the method has been published and subject to peer review; (iii) the error rate; (iv) the existence of standards and whether the witness applied them in the present case; and (v) whether the witness' method is generally accepted as reliable in the relevant medical and scientific community. See Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 594-95.

1. The Daubert Factors Weigh in Favor of Finding that Dr. Jackson's General Causation Methodology is Reliable.

For her methodology, Dr. Jackson relied mainly on peer-reviewed academic literature. Reliance on peer-reviewed academic literature is a permissible way for a medical doctor to establish a methodology for making reliable diagnoses of adverse symptoms – which is what Dr. Jackson attempts to do in her report. To evaluate Dr. Jackson's methodology, the Court must therefore examine the reliability of the studies. To evaluate the reliability of the studies upon which Dr. Jackson relied, the Court must first determine whether the studies and data upon which Dr. Jackson relies meet the standard of Daubert. The Court must then assess whether Dr. Jackson's conclusions flow from her methodology, or whether an insurmountable analytical gap remains.

The Court recognizes that Dr. Jackson has not conducted independent research to arrive at any of her conclusions. Nonetheless, a medical doctor should be able to practice her profession in

a clinical setting by relying on what researchers in her field can learn through scientific study. This methodology is a standard and reliable way for a medical doctor to form opinions and make diagnoses as long as the underlying studies are valid according to scientific standards.

Aside from scientific literature, Dr. Jackson also makes an inference based on two independent observations. First, research shows that Prozac may cause akathasia. Second, akathasia may lead to suicide or homicide. Dr. Jackson, therefore, contends that Prozac may cause suicide or homicide. Aside from evaluating the studies upon which Dr. Jackson relies, the Court must also determine that the inference Dr. Jackson makes is reliable.

a. The Studies upon Which Dr. Jackson Relies Have Been Tested or are Testable.

All of the studies that form a foundation for an opinion in Dr. Jackson's report follow the scientific method. The authors of all of the papers describe their methods, results, implications, and limitations. Each study that Dr. Jackson cites, therefore, is testable because another set of researchers could apply the same criteria and observe whether they achieved similar results.

Some of the papers underlying Dr. Jackson's report involve retrospective statistical analyses of earlier databases. The authors of those papers reveal the formulae that they applied, and other researchers could apply the same formulae to verify the results. The first Daubert factor – testability – therefore, weighs in favor of admitting testimony that relies on the scientific literature underlying Dr. Jackson's report.

Admittedly, there is some difficulty in testing the strength of association between Prozac and suicide by discussing the association between Prozac and akathisia, and between akathisia and suicide. Moreover, Dr. Jackson has not tested the association between these phenomena. The chain of inferences, however, is only part of the reason that she finds a link between Prozac and suicide.

One of the papers that she cites observes suicidality in patients undergoing Prozac therapy. The methods applied in that paper are replicable. The chain-of-events line of reasoning corroborates that study.

b. The Studies upon Which Dr. Jackson Relies are Peer-Reviewed.

The papers upon which Dr. Jackson relies are all peer-reviewed. Therefore, the second Daubert factor also weighs in favor of admissibility. Eli Lilly contends that this factor weighs against Dr. Jackson because the methodology enumerated in Dr. Jackson's report has not been subject to peer-review. That Dr. Jackson's report – or the method it employs – has not been submitted for peer-review, however, is irrelevant. What Dr. Jackson does is uncontroversial. She presents peer-reviewed studies, relies upon, and draws conclusions from those studies. Clinical doctors do something similar when they read scientific studies, and use them to treat patients. Whether the conclusions that Dr. Jackson draws from those papers are valid is a fair question, but to the extent that Dr. Jackson's methodology consists of relying on scientific literature, that literature is peer-reviewed. This safeguard increases the likelihood that the literature is reliable under Daubert v. Merrell Dow Pharmaceuticals, Inc.

c. The Daubert Factors Addressing the Rate of Error, the Existence of Standards, and Whether Dr. Jackson Relied on Them Weigh Against Admission.

Eli Lilly criticizes Dr. Jackson's methodology because Dr. Jackson admitted that she does not know the rate of error of her approach, and because Dr. Jackson did not apply the Hill criteria, which are thought to be standard in determining whether a drug has an adverse effects. Jackson admits that the Hill criteria represent the standard that experts in her field apply for determining whether a drug has a particular adverse effect. See Second Jackson Depo. at 76:22-77:5, id. at 77:15-25. Despite her recognition of those widely accepted criteria, Dr. Jackson did not apply the

Hill criteria to reach any of the conclusions in her report. Moreover, from the record before the Court, it is unclear why Dr. Jackson did not apply the methodology that she recognizes to be standard in her field.

Dr. Jackson not only testified that the Hill criteria are generally accepted in her field. She also asserted that she personally embraced that approach. See id. at 255. That Dr. Jackson chose not to apply the methodology that she personally considers the standard in her field to assess causation undermines the reliability of her testimony. Nonetheless, Dr. Jackson's failure to apply the Hill criteria is not fatal. The existence of one standard that is regarded as optimal is relevant, but Dr. Jackson has applied a methodology that, while perhaps not as reliable as the Hill criteria, is sufficiently reliable and grounded in the scientific method.

Under the Daubert factors, the Court must also assess the degree to which Dr. Jackson's approach is accepted as reliable in the relevant medical and scientific community. Superficially, Jackson's approach is generally accepted to the extent that the approach consists of reading and applying knowledge gained from peer-reviewed literature. Eli Lilly argues, however, that the conclusion that Prozac and suicide are linked is not widely accepted, and that the papers upon which Dr. Jackson relies do not overcome the lack of acceptance because those papers are inherently flawed. Moreover, Eli Lilly points out that Dr. Jackson did not cite any epidemiological studies, and ignored studies that cut against her conclusions.

i. The Human Studies Upon Which Dr. Jackson Relies, While Flawed, Still Present Valid Evidence of General Causation.

Eli Lilly contends that the only two human studies relevant to Prozac's relationship to suicide upon which Jackson relies – the Cusin article and the Perlis article – were uncontrolled. In other words, the subjects upon whom the testing was performed were not compared to another group to

whom a placebo was administered. Dr. Jackson admits that, because of the lack of controlled human studies, one cannot draw a scientifically valid conclusion that Prozac caused or was associated with the observed adverse effects that were reported. See Jackson Depo. at 185-86, 197-98.

Despite this limitation on the usefulness of the uncontrolled human studies, Dr. Jackson relies on these studies to help establish general causation. Under Daubert, scientific opinion testimony must be based in the scientific method. See Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. at 592-93 (internal quotations omitted)("Scientific methodology today is based on generating hypotheses and testing them to see if they can be falsified; indeed, this methodology is what distinguishes science from other fields of human inquiry."). Standing alone, the Cusin and Perlis articles present hypotheses. See Jackson Depo. at 195. It is with that understanding that the authors of both studies conceded that the observed adverse effects may have other causes. Dr. Jackson also admits as much. See Jackson Depo. at 185:24-186.

> Q: And I'm asking you – if you agree with the statement by the authors of the article that you've cited, that worsenings during the first few weeks of treatment may not be etiologically related to antidepressant therapy, but may simply represent a correlate of the natural history of the illness.
>
> A: Oh, I – believe that that is correct.

Id.

Dr. Jackson does not, however, rely solely on the Cusin and Perlis articles. She presents the articles to demonstrate new information concerning the link between Prozac and suicide. The studies are not perfect, but they are based in good science. The authors note the limitations, but that does not undermine the fact that the articles represent evidence of general causation. When considering the articles in light of the other information, including the degree to which the scientific community already accepts a relationship between Prozac and increased suicidality, the Court

cannot say that the flaws inherent in the articles are fatal to Dr. Jackson's testimony. This conclusion remains true, even when those flaws are considered in the aggregate with the other flaws in Dr. Jackson's methodology.

ii. Dr. Jackson's Failure to Rely on Corroborating Epidemiology and her Failure to Deal with Contrary Epidemiology are not Fatal to Her General Causation Analysis.

Eli Lilly cites the Tenth Circuit for the proposition that "epidemiological studies are the best evidence of general causation in a toxic tort case." Motion at 14 (citing Norris v. Baxter Health Care Corp., 397 F.3d at 882). Moreover, the Tenth Circuit has stated that, "[w]hile the presence of epidemiology does not necessarily end the inquiry, where epidemiology is available, it cannot be ignored. As the best evidence of general causation, it must be addressed." Id. While the Tenth Circuit, in Norris v. Baxter Health Care Corp., stated that epidemiological studies are the best evidence in "toxic tort" cases, the Tenth Circuit did not define "toxic tort."

Courts use the term "toxic tort" to refer to circumstances under which plaintiffs attempt to prove that they suffered harm as a result of exposure to a substance. See AM. JUR. NEGLIGENCE § 376. Such a definition would seem to allow for a wide variety of cases, ranging from exposure to harmful external substances, such as nuclear material, to the adverse affects of substances ingested into the body, including prescribed medicines. Nonetheless, the Court need not decide the exact contours of a "toxic tort" to find that the principle that the Court in Norris v. Baxter Health Care Corp. articulated applies in this case.

In Norris v. Baxter Health Care Corp., the Tenth Circuit dealt with plaintiffs who alleged that the contents of medically inserted breast implants caused damaging health effects. See 397 F.3d at 880. In this case, Mark Rimbert argues that the active substance in Prozac caused a damaging health effect – specifically, the substance altered Gilbert Rimbert's brain chemistry in such a way

that it caused him to behave violently and suicidally, against his nature. Moreover, in this case, as in Norris v. Baxter Health Care Corp., the plaintiff must meet the same evidentiary standards respecting the admission of expert opinion. Specifically, the plaintiff must demonstrate general and specific causation with evidence that conforms to rule 702 of the Federal Rules of Evidence. See, e.g., In re Hanford Nuclear Reservation Litigation, 292 F.3d 1124, 1133 (9th Cir. 2002)("Causation in toxic tort cases is typically discussed in terms of generic and specific causation."). Finally, the Tenth Circuit, in Norris v. Baxter Health Care Corp., relied at least in part on a pharmaceuticals case – involving Benedictin – to articulate its standard. See Norris v. Baxter Healthcare Corp., 397 F.3d at 881 (citing Raynor v. Merrell Pharm., Inc., 104 F.3d 1371, 1376 (D.C. Cir. 1997), for the proposition that "causation in toxic tort cases is discussed in terms of general causation and specific causation."). The Court will therefore follow Norris v. Baxter Health Care Corp. in treating this case as one for a toxic tort, at least for purposes of determining the admissibility of an expert.

Dr. Jackson not only failed to rely on an epidemiological study to prove her conclusions. She also ignored epidemiological studies that support the contrary. For example, in the December 13, 2007 deposition, Dr. Jackson was asked whether she was aware of "a body of published medical literature, including controlled clinical trials and epidemiological studies, that stands for the proposition that, in fact, ingestion of Prozac is not associated with suicidality[.]" Jackson Depo. at 66:11-15. Dr. Jackson responded that she was "aware of that argument," but that she did not read or consider that literature in preparing her report. Id. at 17-22.

While the Tenth Circuit has stated that epidemiological evidence is the best evidence of general causation, it did not hold that such evidence is always required. Norris v. Baxter Health Care Corp. dealt with breast implant litigation where "the body of epidemiology largely f[ound] no association between silicone breast implants and immune system diseases." 397 F.3d at 882. For

that reason, the Tenth Circuit stated that, "where there is a large body of contrary epidemiology evidence, it is necessary to at least address it with evidence that is based on medically reliable and scientifically valid methodology." Id. "While the presence of epidemiology does not necessarily end the inquiry, where epidemiology is available, it cannot be ignored." Id. The Tenth Circuit summarized its view, stating: "We are not holding that epidemiological studies are always necessary in a toxic tort case. We are simply holding that where there is a large body of contrary epidemiological evidence, it is necessary to at least address it with evidence that is based on medically reliable and scientifically valid methodology." Norris v. Baxter Healthcare Corp., 397 F.3d at 882 (emphasis added).[7]

In this case, in accordance with Norris v. Baxter Healthcare Corp., the contrary epidemiological evidence has been sufficiently addressed to survive a Daubert challenge. Dr. Jackson used a scientifically valid methodology in her causation analysis. She relied on peer-reviewed literature and made permissible inferences based on that literature. The Court also observes that large-scale epidemiological studies exist to corroborate Dr. Jackson's causation analysis, even if Dr. Jackson did not rely on epidemiology. Where multiple large-scale epidemiological studies exist to support Dr. Jackson's general causation methodology, Norris v. Baxter Healthcare Corp. does not command that her testimony be excluded. Unlike the proposed expert testimony in Norris v. Baxter Healthcare Corp., Dr. Jackson is not testifying against a tide of scientific consensus. Cf. Wilson v. Merrell Dow Pharmaceuticals, Inc., 893 F.2d 1149, 1154

[7] The Tenth Circuit did not indicate whether the expert, the parties, or the district court had to address the contrary epidemiological evidence. Certainly, the Court and the parties have addressed the contrary epidemiological studies. The Court does not believe the Tenth Circuit in Norris v. Baxter Healthcare Corp. held it was essential that the expert do so where, as here, there are large-scale epidemiological studies to support her conclusions, and where the expert expressly relies on other non-epidemiological scientific evidence to support the expert's conclusions.

(10th Cir. 1990)(finding sufficient evidence to support a jury verdict in favor of the defendant where the defendant "presented expert testimony, which was not contradicted by the [plaintiff's] experts, that of the approximately forty epidemiological studies of Bendectin, none has shown a statistically significant association between ingestion of the drug and incidence of birth defects generally or limb defects in particular").

The experts in Norris v. Baxter Healthcare Corp. testified on the basis of their own "case series with sequential observations in many patients" and differential diagnosis. 397 F.3d at 884-85. The experts could not articulate why their opinions ran contrary to the body of evidence. See id. at 885. Instead, the experts explained the lack of scientific evidence in their favor by stating that the phenomenon they described had escaped study. See id. Both the district court and the Tenth Circuit found their explanation to be insufficient. See id. Additionally, the Tenth Circuit noted that differential diagnosis "assumes that general causation has been proven." Id. (citations omitted)(emphasis in original). The experts' reliance on differential diagnosis absent proof of general causation was misplaced. See id. The Tenth Circuit observed that the "[p]laintiff's experts' differential diagnoses and case studies are scientifically unreliable because they assume what science has largely shown does not exist – a causal connection between silicone breast implants and disease." Id. at 886.

In contrast to Norris v. Baxter Healthcare Corp., this case involves a phenomenon that the scientific community has not "largely shown" to be non-existent. The scientific community has not reached a consensus, but it has recognized some causal connection. Many studies, including epidemiological studies, exist to corroborate the existence of a link between Prozac and suicide. Moreover, Dr. Jackson went further than merely to rely on her own case studies and differential diagnosis. She discussed general causation and cited independent, scientific studies to support her

assertions. Dr. Jackson, therefore, does not necessarily need to provide epidemiology.

Nevertheless, it is troubling that Dr. Jackson has ignored epidemiological studies which suggest that her conclusions are incorrect. This disregard of unfavorable epidemiological studies leaves a missing step in the analysis which must be filled with valid scientific evidence. The Court finds sufficient evidence, however, to close the gap.

First, apart from the animal studies and the non-controlled human studies upon which she relies, Dr. Jackson quotes a standard manual for diagnosis of mental disorders, which states that "[a]kathisia may be associated with dysphoria, irritability, aggression, or suicide attempts . . . . Serotonin-specific reuptake inhibitor antidepressant medications may produce akathisia that appears to be identical in phenomology and treatment response to Neuroleptic-Induced Acute Akathisia." See Report at 37 (quoting the DSM at 801). That a relationship between the SSRIs, akathisia, and suicide is sufficiently understood to document it in the standard manual suggests a high degree of acceptance in the scientific community.

Admittedly, one district court has rejected this "chain-of-events" line of reasoning. See Miller v. Pfizer, Inc., 196 F.Supp.2d at 1080.[8] The district court in that case explained:

> Generally accepted methodology . . . required [the expert] to consistently test the strength of association between SSRI drugs and suicide (the outcome of interest) -- rather than the association between SSRI drugs and akathisia (which is purported to be part of the chain of events that lead to suicide, rather than an independent outcome) . . . .

Id. The Court finds, however, that this case is distinguishable from Miller v. Pfizer. Unlike the

[8] On appeal, the United States Court of Appeals for the Tenth Circuit affirmed the district court's exercise of discretion to exclude the expert's testimony. See Miller v. Pfizer, Inc., 356 F.3d at 1335 ("[T]o the extent that the [plaintiffs] argue that the district court abused its discretion in applying the gatekeeper standard, we find no abuse of discretion."). The Tenth Circuit neither endorsed nor rejected the district court's reasoning on whether the "chain of events" approach was proper. See id.

expert in Miller v. Pfizer, Dr. Jackson provides more than just logic to support her contention that links exist between SSRIs and akathisia, and between akathisia and suicide. She relies on the DSM, which is "the standard classification of mental disorders used by mental health professionals in the United States." American Psychiatric Association, http://psych.org/MainMenu/Research/DSMIV.aspx (last visited September 25, 2008).

Second, other studies and materials, including epidemiological studies, have been brought to the Court's attention which corroborate the contention that a link between SSRIs and suicide – which is at the heart of Dr. Jackson's general causation theory – has gained broad acceptance. First, the FDA has recognized a connection, at least for certain age-groups. The FDA warning label for Prozac summarizes studies showing as much. The label, which relies on epidemiological evidence, states:

> Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder and other psychiatric disorders. Anyone considering the use of Prozac or any other antidepressant in a child, adolescent, or young adult, must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain psychiatric disorders are themselves associated with increases in the risk of suicide.

FDA Warning at 1. Despite the age limitation, the warning also advises that all patients undergoing treatment with Prozac should be monitored closely for clinical worsening or suicidality – especially in the first few months. Id. at 11. The significance of the FDA's warning is that the FDA has recognized a link between Prozac, and suicidality and other adverse affects. The FDA's recognition of such a link is evidence of the level of acceptance that the Prozac-suicidality link has gained in the scientific community. Even if the significant age limitation cuts against the facts in this case, other material suggests the existence of a link in adults as well.

The other studies that Mark Rimbert brought to the Court's attention also go far to indicate the level of acceptance that Dr. Jackson's general causation analysis has attained. For example, the Jick article discusses a large-scale epidemiological study involving 172,598 participants. See Jick Article at 215. The study showed that fluoxetine had a rate of suicidality substantially higher than other anti-depressants. See id. at 218. Moreover, the Jick article showed that fluoxetine's relative risk level was consistently 2.1 or greater. Other studies suggest that Prozac carries a suicide risk in adults as well as children. See I. Aursnes, I. F. Tvete, J. Gaasemyr & B. Natvig, Suicide Attempts in Clinical Trials with Peroxetine Randomized Against Placebo, 3 BMC MEDICINE 14 (2005)("Patients and doctors should be warned that the increased suicidal activity observed in children and adolescents taking certain antidepressant drugs may also be present in adults.")("Aursnes Article"); D. Fergusson, S. Doucette, K. C. Glass, S. Shapiro, D. Healy, P. Hebert & B. Hutton, The Association Between Suicide Attempts and SSRIs: A Systematic Review of Randomized Controlled Trials, 330 BMJ 396. One large epidemiological study, which focused on individuals belonging to Gilbert Rimbert's age-group, showed that "SSRI antidepressants were associated with a nearly fivefold higher risk of completed suicide than other antidepressants." Exhibit 9 to Plaintiff's Response Memorandum in Opposition to Defendant's Motion for Summary Judgment on all Claims (filed April 17, 2008)(Doc. 74)("Response"), D. Juurlink, M. Mamdani, A. Kopp, D. Redelmeier, The Risk of Suicide with Selective Serotonin Reuptake Inhibitors in the Elderly, 163 AM. J. PSYCHIATRY 813, 813 (2006)("Juurlink Study").

The Court recognizes that Eli Lilly objected to any review of these additional materials, upon which Dr. Jackson did not rely in preparing her report. The Court, however, finds it appropriate to examine the materials for the purpose of determining the level of acceptance that Dr. Jackson's general causation methodology enjoys, and whether there is sufficient evidence of a link between

Prozac and suicidality to close the analytic gap that Jackson's report arguably leaves open. The Court finds that the studies so indicate. Moreover, while the Court reviews the extra materials to inform its decision, the Court does not hold that Dr. Jackson may rely on those materials extraneous to her report in testifying at trial.

The Daubert factors generally weigh in favor of admitting Dr. Jackson's testimony on general causation, despite some of the flaws inherent in her methodology. When Dr. Jackson's report is read in the context of the supplemental studies, her conclusions on general causation are sufficiently accepted within the scientific community, and thus reliable to allow her to testify concerning them. Given that the FDA has recognized a link between SSRIs and suicidality, the Court should be reluctant to preclude Dr. Jackson from at least testifying as far as the FDA has been willing to go.

2. Dr. Jackson's Specific Causation Analysis is Reliable Under Daubert.

To establish specific causation, Dr. Jackson performed a "differential diagnosis" in light of three factors: pharmacodymanics, pharmacokinetics, and Gilbert Rimbert's unique biology. Differential diagnosis, if properly applied, is a valid technique for determining specific causation. See Goebel v. Denver and Rio Grande Wester R. Co., 346 F.3d 987, 998(10th Cir. 2003)(citations omitted)("[A] reliable differential diagnosis is admissible in this circuit given a valid showing of general causation."). Moreover, the three factors that Dr. Jackson proposes to consider are proper and relevant to an inquiry of the effect that Prozac had on an individual. The approach that Dr. Jackson proposes is similar to what one would expect for a medical diagnosis – which is essentially what Dr. Jackson is being asked to do. The more material question, therefore, is not whether Dr. Jackson employed a valid technique, but whether Dr. Jackson properly applied that technique in a reliable manner. The Court finds that Dr. Jackson's application of her technique is sufficiently

reliable and based in science to withstand a challenge under Daubert v. Merrell Dow Pharmaceuticals, Inc.

First, the underlying data upon which Dr. Jackson relies is scientifically sound. She cites various articles from peer-reviewed journals to establish the effects that Prozac has on the brain, and the manner in which the human body absorbs, distributes, metabolizes, and eliminates Prozac. Some of the articles to which she refers are about human studies, while others deal with animal studies. Relying on these studies, Dr. Jackson examined Gilbert Rimbert's medical history, physical characteristics, and other factors that might have contributed to his final outburst.

Eli Lilly points out various flaws with the animal data. Eli Lilly asserts that the conclusions that Dr. Jackson extrapolates from the animal studies cited in her report do not rise above the level of hypothesis. In her report, Dr. Jackson states: "In vivo animal studies have shown that SSRIs eventually reduce the brain's supply of releasable serotonin. Postmortem analyses of animals exposed to SSRIs have confirmed a 50-70% depletion of serotonin." Report at 44. Moreover, she states: "Electrochemical studies in animals have shown that acute exposure to SSRIs is accompanied by reduced firing rates of serotonin and dopamine neurons. The early suppression of dopamine activity with the brainstem. . . is believed to account for akathisia and other side effects which can lead to aggression and suicide." Id. Dr. Jackson concedes, however, that the animal studies do no more than create hypotheses:

> Q: . . . The animal studies, the rat brain and monkey brain studies that you cite in your report, they do not prove the effects cited in those studies actually happened in humans, do they?
>
> A: They don't prove it.
>
> Q: They simply create various hypotheses, right?
>
> A: That's correct

Exhibit B to Memo. in Support of Motion to Exclude, Deposition of Dr. Jackson at 269-70 (taken February 11, 2008)("Third Jackson Depo.").

Forming a hypothesis is a valid part of the scientific method, but Dr. Jackson admits it represents only the beginning of a process. See Jackson Depo. at 157. The Court does not question the scientific basis underlying the animal studies. Those studies appear to have been conducted under rigorous standards. The concern is that these studies relate to Jackson's conclusions about issues in this case only by way of hypothesis.

To scientifically link them directly to the question at issue in her report – whether Prozac causes suicidal and/or violent behavior in humans – requires testing. Again, Jackson admits this need. See id. at 269-70.

> Q: They create various hypotheses, right?
>
> A: That's correct.
>
> Q: That are tested and can really only be tested by doing the same kind of study in human beings?
>
> A: That would be the best way, correct.
>
> Q: The only way, would it?
>
> A: To verify it in humans, yes.

Id.

Despite these weaknesses in the animal studies, the Court finds that they do not undercut Dr. Jackson's testimony to the point of making it non-scientific and unreliable. The animal studies are present to corroborate data from human studies, which Dr. Jackson also cites in her report. The Court might be more concerned if Dr. Jackson merely attempted to extrapolate from the animal data to human beings without any testing or corroboration. In this case, however, Dr. Jackson relied on

human and animal studies. In discussing the implications of the animal data, Dr. Jackson states: "These findings [in the animal studies] from neuroscience corroborate the results of monoamine depletion studies in human subjects. In other words, serotonin reuptake inhibitors appear to induce long-lasting vulnerability within the serotonin pathways of the brain – a perturbation which likely increases the risk of chronic and/or recurrent depression and anxiety." Report at 44.

Dr. Jackson also points to human studies that demonstrate the association between low levels of the serotonin metabolyte 5HIAA in the spinal fluid, and impulsivity, aggression, and suicide. See Report at 38 (citing J. Fawcett, K. Busch, D. Jacobs, H. Kravitz, & L. Fogg, Suicide: A Four-pathway Clinical-Biochemical Model, 836 ANNALS NEW YORK ACADEMY OF SCIENCES 288 (1997); J. Mann & D. Currier, A Review of Prospective Studies of Biological Predictors of Suicidal Behavior in Mood Disorders, 11 ARCHIVES OF SUICIDE RESEARCH 3 (2007); J. Mann, V. Arango, P. Marzuk, S Theccanat, & D.J. Reis, Evidence for the 5-HT Hypothesis of Suicide: A Review of Post-mortem Studies, 155 BRITISH J. PSYCHIATRY 7 (1989 (Supp. 8); L. Ricci & M. Wellman, Monoamines: Biochemical Markers of Suicide?, 46 J. CLINICAL PSYCHOLOGY 106 (1990); V. Linnoila & M. Virkkunen, Aggression, Suicidality, and Serotonin, J. CLINICAL PSYCHIATRY 46 (1992)(Supp)). In conjunction with the animal studies, Dr. Jackson may validly draw conclusions from the body of literature upon which she relies to support her conclusion about the role of Prozac in this case.

Eli Lilly contends that Dr. Jackson's opinion does little more than present possibilities about the effects of Prozac and does not eliminate other possible causes for Gilbert Rimbert's outburst. See Motion at 22. From the report, Gilbert Rimbert seems to have been a man in trouble. He was lonely and unsatisfied, and his wife was in the process of leaving him and ending a marriage that had long gone cold. He was distressed because of the impending divorce. Moreover, he suffered

from various frustrating physical ailments, including diabetes and impotence. See Report at 31. As Dr. Jackson states in her report: "Protective factors against suicide were minimal." Id.

Eli Lilly maintains that, using a reliable differential diagnosis, Dr. Jackson should be able to systematically rule out these other risk factors of depression, or at least show that they had less to do with Gilbert Rimbert's actions than his ingestion of Prozac. See Motion 24. Eli Lilly argues that, because Dr. Jackson cannot rule out the other causes, her testimony will not be helpful to the jury. See id. at 29.

Dr. Jackson's testimony need not, however, eliminate other factors to form a valid conclusion. The Tenth Circuit has stated that an expert does not need to "categorically exclude each and every possible alternative cause . . ." to offer an expert opinion on causation. Especially under circumstances as complex as an alleged medication-induced violent outburst, causation will involve numerous elements working together, and it is sufficient that the expert can reasonably make a medical judgment that Prozac was a substantial cause, even if the ultimate result occurred because of the existence of other risk factors combined with the Prozac.

Dr. Jackson's opinion about specific causation is that multiple factors, including the stressors in Gilbert Rimbert's life, his physical characteristics, and the manner in which Prozac allegedly affects the mind and body, contributed to Gilbert Rimbert's final outburst. See Report at 50. In the final paragraph of her report, Dr. Jackson wrote:

> Based upon the facts of the case as they have been presented to me, and based upon my understanding of the neurobehavioral effects of Prozac, I believe that it would be incorrect to suggest that Prozac was the necessary and sufficient cause of deaths of Gilbert and Olivia Rimbert, and their pet dog (Ivy). However, in the context of Gilbert's pre-existing risk factors for suicide and homicide, and in the context of his diminished capacity to resist them, it is more likely than not true that Prozac converted a case of probable dysthymia into a case of agitated depression with obsessive and psychotic features. In this sense, Prozac was the definitive, contributive cause of the Rimbert tragedy.

Id. Dr. Jackson has further and properly clarified her position that "it was against a complex backdrop of personal and familial circumstances, but within a progressive chain of events, that Prozac proved to be the 'clincher.'" Jackson Aff. at 4. Dr. Jackson has also stated under oath, that she believes, to within a reasonable degree of medical certainty, that Prozac contributed to the Rimbert tragedy. See Jackson Depo. at 359-60. This opinion on specific causation is sufficiently reliable, and is based, not on mere speculation, but on a sophisticated medical diagnosis and analysis.

In forming her opinion, Dr. Jackson did what one would expect a medical doctor to do when presented with a symptom, or set of symptoms, and the various other associated data. She applied her medical judgment, based on her own medical training, peer-reviewed scientific literature on point, and other valid, logical inferences, to explain the symptoms. Dr. Jackson can demonstrate with clarity how she arrived at her conclusions, and another expert can evaluate her performance and, if so inclined, disagree. In this case, considering that Dr. Jackson meets the minimum requirements for offering expert testimony, the proper forum to disagree with her testimony now becomes the courtroom with cross-examination. Eli Lilly can also put on its experts, if those experts are qualified, and offer admissible testimony.

As a general matter, the Court observes that to exclude Dr. Jackson's testimony because it does not eliminate depression and other life stressors as a possible cause would create a nearly insurmountable barrier in products-liability cases involving anti-depressants. Antidepressants are typically – although admittedly not always – prescribed to treat depression. Thus, plaintiffs alleging Prozac-induced suicide would nearly always have a background of depression, and perhaps pre-existing suicide stressors. If Prozac truly did, as Mark Rimbert alleges, push such an individual over

the edge, the individual, or his or her personal representatives, would almost never be able to eliminate depression as the cause of the suicide. The best that can be expected is to show that, but-for the anti-depressant, the alleged outburst would not have occurred in the specific individual's case. Mark Rimbert is trying to establish this principle, and if expert testimony can make a scientific argument that Prozac substantially caused, even against a complex backdrop of other dangerous factors, the outburst, then the Court should allow that expert to testify as to specific causation.

In conclusion, the Court finds that Dr. Jackson's testimony, while flawed in certain respects, meets the standards for admissibility under Daubert v. Merrell Dow Pharmaceuticals, Inc. Dr. Jackson's testimony is sufficiently reliable, and will therefore be helpful to the jury.

IT IS ORDERED that Defendant Eli Lilly and Company's Motion to Exclude Expert Testimony of Dr. Grace Jackson is denied.

UNITED STATES DISTRICT JUDGE

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